Abstract for Results of CAOLD Search


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=> d que
L5          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("CA55:23481E"/OREF OR
               "CA56:434G"/OREF OR "CA56:453C"/OREF OR "CA56:8660I"/OREF OR
               "CA58:11311F"/OREF OR "CA59:2745E"/OREF OR "CA60:10626B"/OREF)
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Caold answer 1

L5 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN 1964:60733 HCAPLUS
DN 60:60733
OREF 60:**10626b-h,10627a-e**
TI Substances acting on the central nervous system. XXXIII. 3-Hydroxymethyl-3-phenylazetidine and derivatives
AU Testa, Emilio; Fontanella, Luigi; Bovara, Mario
CS Lepetit S.p.A., Milan
SO (1964) 97-106
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. CA 59, 12735h; 60, 6847f. I (R = R' = H) (II) and a no. of its derivs. were prepd. for pharmacol. investigation. To a suspension of 32 g. LiAlH4 in 500 cc. tetrahydrofuran (THF) was added slowly dropwise at below 20.degree. a 10%, soln. of 38 g. 3-hydroxymethyl-3-phenyl2-azetidinone (IIa) in THF and the mixt. refluxed 8 hrs. to give 17.85 g. II, m. 135-7.degree.(EtOAc); HCl salt m. 211-12.degree. (EtOH). Phthalimide (2.26 g.) in 40 cc. 95% EtOH heated 5 min. at 60-70.degree. with 4.39 cc. 39% aq. HCHO, the soln. treated dropwise at 60-70.degree. with 2.5 g. II in 35 cc. EtOH, boiled 30 min., filtered hot, and concd. in vacuo, the oily residue dissolved in 100 cc. abs. Et2O, and the soln. filtered and treated with satd. Et2O-HCl gave 3.08 g. I (R = phthalimidomethyl, R' = H) HCl salt, m. 165-7.degree. (EtOH). 3,3-Diisopropyl-2,4-azetidinedione (3.1 g.), 35 cc. EtOH, 1.8 cc. 39% aq. HCHO, and 3 g. II in 60 cc. EtOH treated similarly gave 6.1 g. I (R = 3,3-diisopropyl-2,4-dioxoazetidinylmethyl, R' = H), m. 90-2.degree. (aq. EtOH). II.HCl (2 g.) and 650 mg. NaOCN in 20 cc. H2O heated 15 min. at 60.degree. and refrigerated overnight gave 1.5 g. I (R = CONH2, R' = H) (III), m. 180-2.degree. (abs. EtOH). III (900 mg.) in 25 cc. CHCl3 treated at 0.degree. with stirring with 400 mg. NaOCN under anhyd. conditions followed by dry HCl (1 hr.) and 400 mg. NaOCN added followed by dry HCl (1 hr.) gave 120 mg. I (R = R' = CONH2), m. 2213.degree. (H2O). II (2 g.) in 30.degree. cc. abs. PhMe treated dropwise with 2.8 g. PhNCO, and the mixt. heated 15 min. at 50.degree. and cooled to 0.degree. gave 3.1 g. I(R = CONHPh, R' = H), m. 211-12.degree. (abs. EtOH). II (10 g.) dissolved in 60 cc. cold N H2SO4, the soln. treated gradually at 0-5.degree. with 5.4 g. NaNO2 with stirring, let warm up slowly, heated 30 min. on a water bath, treated with 2 g. NaNO2, boiled 15 min., and cooled, and the product isolated with EtOAc-Et2O gave 7 g. I (R = NO, R' = H) (IV), m. 72-5.degree. (Et2O). To a cold (0-5.degree.) suspension of 580 mg. LiAlH4 in 20 cc. THF was added slowly 2 g. IV in 20 cc. THF with stirring and the mixt. heated slowly to 45.degree. and stirred 2 hrs, at 45.degree. to give 660 mg. I (R = NH2, R' = H), m. 109-12.degree. (EtOAc); pnitrobenzylidene deriv. m. 122-3.degree. (abs. EtOH). To a suspension of 2 g. II.HCl in 10 cc. AcOH was added 1.1 cc. AcCl at 20.degree. and the mixt. let stand 24 hrs. to give 2.1 g. I (R = H, R' = Ac) HCl salt, m. 145-7.degree. (MeOH-Et2O), (Method A) II (2.5 g.) in 5 cc. pyridine treated dropwise with 2.5 cc. (EtCO)2O (V) with icesalt cooling, the soln. let warm up slowly, kept overnight at 20.degree., dild. with 15 cc. EtOH, boiled 15 min., and evapd. in vacuo, the residue dissolved in 2N HCl, the soln. extd. with Et2O, and the extd. distd. gave 1.7 g. I (R = R' = EtCO) (VI), b0.4 175-85.degree. (air bath). (Method B) II (3.5 g.) and 10 cc. V heated 30 min. at 130.degree. and the mixt. cooled to 80.degree., dild. with 30 cc. EtOH, heated 30 min. at 80-90.degree., and then processed by method A gave 4.34 g. VI, b0.4 175-85.degree. (air bath). From II and

Ac2O was prepd. by method B 71% I (R = R' = Ac) (VII), m. 104-5.degree. (Et2O). From II and BzCl was prepd. by method A 74% I (R = R' = Bz) (VIIa), m. 98-100' (Et2O). VII (7.9 g.) in 13 cc. MeOH kept overnight at 20.degree. with 13 cc. 10% aq. KOH, the soln. evapd. in vacuo, the residue extd. with EtOAc, and the ext. concd. to small vol. deposited 5.01 g. I (R = Ac, R' = H) (VIII), m. 119-21.degree. (EtOAc). Crude II (obtained by redn. of 109 g. IIa with 65 g. LiAlH4) dissolved in 10% HCl, and the soln. extd. with EtOAc and made alk. with 50% aq. NaOH gave 66 g. VIII, m. 120-1.degree. (EtOAc). VIII (1.16 g.) in 25 cc. 10% HCl refluxed 45 min., the soln. evapd. in vacuo, and the residual solid repeatedly evapd. with EtOH gave 1.05 g. II.HCl, m. 210-12.degree. (EtOH). VI hydrolyzed like VII gave 91% I(R = Pr, R' = H), m. 76-7.degree. (Et2O). II (4 g.) dissolved in 2.26 g. HCO2H under cooling after 2 min. 800 mg. 35% aq. HCHO added, followed by 4 cc. H2O, the soln. heated slowly, boiled 2 hrs., treated with 6 cc. 12N HCl at the b.p., and after 5 min. concd. in vacuo, and the residual oil repeatedly evapd. with MeOH and crystd. from MeOH-Et2O gave 1.2 g. I (R = Me, R' = H) HCl salt (IX.HCl), m. 151-3.degree. (EtOHEt2O); IX m. 96-7.degree. (sublimation at 60.degree./2 mm.); picrate m. 1579.degree. (EtOH) methiodide, m. 182-3.degree. (Et2O). To a suspension of 1 g. LiAlH4 in 50 cc. Et2O was added dropwise 1.5 g. VII in 100 cc. Et2O with stirring and cooling and the mixt. slowly brought to the b.p. and refluxed 3 hrs. to give 1.05 g. I(R = Et, R' = H) (IXa), m. 90-1.degree. (Et2O); HCl salt m. 158.degree. (EtOH-Et2O); picrate m. 125-7.degree. (EtOH); methiodide m. 113-15.degree. (Et2O). To a stirred suspension of 15 g. LiAlH4 in 200 cc. Et2O was added dropwise 21 g. VIIa in 400 cc. Et2O with cooling to give 14.6 g. I (R = PhCH2, R' = H) HCl salt (X.HCl), m. 148-50.degree., which (500 mg.) was dissolved in 10 cc. cold H2O and treated with N NaOH to give 355 mg. X, m. 89-91.degree. (C6H6-petr. ether); meth- iodide, m. 143.degree. (Me2CO-Et2O). Very finely powd. NaOCN (1.2 g.) added to 3 g. IX in 50 cc. dry CHCl3 at 0.degree. (anhyd. conditions), the mixt. treated with dry HCl at 0.degree., treated with 1.2 g. finely powd. NaOCN, followed by dry HCl for 1 hr., stirred 1 hr. at 0.degree., and extd. with H2O, and the aq. soln. extd. with EtOAc and made alk. with N NaOH under cooling gave 2.4 g. I (R = Me, R' = H2NOC), m. 119-22.degree. (Et2O). From IXa and X and NaO- CN were similarly prepd. 67% I (R = Et, R' = H2NOC), m. 93-5.degree. (methiodide m. 177-8.degree.), and 63% I (R = PhCH2, R' = H2NOC), m. 101-2.degree. (Et2O), resp. IX.HCl (3.5 g.) in 15 cc. AcOH treated slowly with 2.15 cc. EtCOCl and the soln. let stand 24 hrs. gave 3.15 g. I (R = Me, R' = EtCO) HCl salt (XI.HCl), m. 149-51.degree. (Me2CO); XI, viscous oil, b0.2 80-5.degree. (air bath). IXa and X treated similarly with EtCOCl gave 79% I (R = Et, R' = EtCO) HCl salt, m. 155-7' (Me2CO), and 61% I (R = PhCH2, R' = EtCO), b0.4 160.degree. (air bath) [picrate m. 125-7.degree. (Et2O); H maleate m. 140-2.degree. (EtOAc)], resp. IXa (3 g.) in 9 cc. Ac2O heated 30 min. at 120.degree., the soln. cooled to 80.degree., treated with 20 cc. EtOH, boiled 15 min., and evapd. in vacuo, and the residue extd. with Et2O gave 2.95 g. AcNEtCH2CPh- (CH2OAc)2 (XII), m. 79-80.degree. (iso-Pr2O). XII (3.3 g.) in 50 cc. 10% HCl refluxed 45 min. gave 1.2 g. (HOH2C)2CPhCH2NH- Et. HCl (XIII.HCl), m. 116-18.degree.. To a suspension of 12 g. Li- AlH4 in 150 cc. Et2O was added dropwise 18 g. AcHNCH2CPh (CH2OH)CO2Et in 250 cc. Et2O with stirring and cooling and the mixt. boiled 6 hrs. to give 9.7 g. XIII, b0.2 140-5.degree. (air bath), converted to 5.9 g. XIII.HCl, m. 116-18.degree. (Me2CO).

XXXIV.3-Hydroxy-3-phenylazetidine. Emilio Testa and Luigi Fontanella. Ibid. 106-8. To EtMgBr soln. was added dropwise during 3 hrs. 50 g. H2NCH2CPh(OH)CO2Et in 3 l. dry Et2O at below 25.degree. with stirring and the soln. refluxed 3 hrs. and kept overnight to give 5.25 g.

3-hydroxy-3-phenyl-2-azetidinone, (I), m. 136-8.degree. (Et2O). To 7 g. LiAlH4 suspended in 150 cc. abs. tetrahydrofuran (THF) was added dropwise 9.6 g. I in 150 cc. THF at below 20.degree. with stirring and the mixt. refluxed 4 hrs. to give 8.1 g. 3-hydroxy-3-phenylazetidine (II) H oxalate (III), m. 190-2.degree. (decompn.) (1:1 EtOH-MeOH). III (4 g.) dissolved in the least possible amt. H2O, the soln. made alk. with 50% aq. NaOH in the cold, satd. with NaCl, and extd. repeatedly with Et2O, and the combined exts. dried, concd. to 30 cc., and cooled to 0.degree. gave 2.1 g. II, m. 160-2.degree. (1: 1 Et2O-EtOAc).

L5 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2002 ACS

CAOLD Ans. 2

AN 1963:415448 HCAPLUS

DN 59:15448

OREF 59:**2745e-h,2746b-h**

TI Substances acting on the central nervous system. XXVI. Chemistry of 3,3-disubstituted azetidines. 3.

AU Testa, Emilio; Fontanella, Luigi; Mariani, Luigi

CS Lepetit S.p.A., Milan, Italy

SO Ann. (1962), 660, 135-43

DT Journal

LA Unavailable

GI For diagram(s), see printed CA Issue.

AB cf. CA 55, 6460a, 27270i; 59, 1521c. Derivs. of azetidine (I) were prepd. ClCH2CH2COCl (9.8 g.), 17 g. Et3N (II), and 12.5 g. 3-phenyl-3-ethylazetidine (III) in 30 cc. abs. Et2O at 0-5.degree., held 1 hr. at 0.degree., and acidified with cold dil. HCl yielded on isolation 14 g. crude N-(.beta.-chloropropionyl)-3-phenyl-3-ethylazetidine (IV) (decompd. on distn.), which on refluxing 4 hrs. with 4.42 g. Et2NH and 11.2 g. II in 30 cc. abs. C6H6, yielded on isolation an oil. The oil was taken up in Et2O, decolorized with C, and treated with citric acid in Et2O to give a ppt. of 15.2 g. N-(.beta.-diethylaminopropionyl)-3-phenyl-3-ethylazetidine citrate, m. 142.degree. (EtOAc-MeOH). IV (14 g.), 4.85 g. morpholine, 11.2 g. II, and 30 cc. abs. C6H6 was refluxed 4 hrs. and similarly gave an Et2O soln., which with gaseous HCl yielded 9.3 g. N-(.beta.-morpholinopropionyl)-3-phenyl-3-ethylazetidine hydrochloride, m. 165-8.degree. (EtOAc-MeOH). MeCH(OAc)COCl (9.33 g.) slowly added to a soln. of 10 g. III and 12.5 g. II in 30 cc. abs. C6H6 at 0.degree. and after 2 hrs. poured into ice water yielded on isolation an oil. Hydrolysis of the oil by refluxing 30 min. with 170 cc. satd. NaHCO3 and 170 cc. MeOH gave 7.1 g. N-(.alpha.-hydroxypropionyl)-3-phenyl-3-ethylazetidine, m. 79-81.degree. (ligroine). 3-Phenyl-3-isopropylazetidine (7 g.) was treated with cooling with 21 cc. (EtCO)2O (V), heated 60 min. at 115-20.degree., cooled to 60.degree., poured into 150 cc. lukewarm H2O, cooled to 0.degree. adjusted to pH 8-9, extd. with Et2O, washed with 10% NaOH and then H2O to yield 90% N-propionyl-3-phenyl-3-isopropylazetidine, b0.4 140.degree.. Reaction of 5 g. 3-phenyl-3-butylazetidine with V similarly gave 89% N-propionyl-3-phenyl-3-butylazetidine, b0.6 150.degree.. NaOEt from 23 g. Na and 100 cc. abs. EtOH in 350 cc. abs. PhMe, 117 g. PhCH2CN, and 236 g. (EtO)2CO (VI) was distd. slowly until the b.p. reached 110-12.degree., the residue cooled to 40.degree., 136 g. Et2NCH2CH2Cl and 250 cc. abs. EtOH added, refluxed 90 min., evapd, in vacuo to 300 cc., 200 cc. H2O added, extd. with Et2O, the Et2O ext. washed with 10% NaOH and then H2O to yield on distn. 250 g. ethyl .alpha.-phenyl-.alpha.-(.beta.-diethylaminoethyl)-.alpha.-cyanoacetate, b1.5 147-51.degree. (VII). VII (150 g.) was reduced with H at 50 atm. in 250 cc. abs. EtOH and 70 g. Raney Ni at 70-80.degree. to yield on isolation and distn. 70% ethyl .alpha.-phenyl-.alpha.-(.beta.-

diethylaminoethyl)-.beta.aminopropionate (VIII), b0.3 134-6.degree.. VIII (140 g.) in 280 cc. abs. Et2O was dropped into a Grignard soln. (from 42 g. Mg, 250 g. MeI, and 720 cc. abs. Et2O) at 20-5.degree., after 1 hr. cooled to 0-5.degree., and acidified. The aq. layer was alkalinized with 10% NaOH, filtered, and extd. with Et2O to give on distn. 16% 3-phenyl-3(.beta.-diethylaminoethyl)azetidin-2-one (IX), b0.4 138-45.degree.. IX (10.9 g.) and 6.4 g. LiAlH4 in abs. Et2O was refluxed 4 hrs., cooled to 0.degree., treated with 50 cc. 20% NH4Cl soln., followed by isolation and distn, of the product yielded 31% 3-phenyl-3-(.beta.diethylaminoethyl)azetidine (X), b0.4 125-30.degree.. X (3.1 g.) and 6.5 g. V were allowed to react and the product isolated to yield 20% N-propionyl-3-phenyl-3-(.beta.-diethylaminoethyl)azetidine, b0.4 160-5.degree.. p-MeC6H4CH2CN (111 g.) added to a soln. of Na-OEt from 19.5 g. Na and 76 cc. abs. EtOH in 300 cc. abs. PhMe at 50.degree., 200 cc. VI and 50 cc. abs. PhMe added, the soln. slowly distd. 4 hrs. until the b.p. reached 110.degree., cooled to 40.degree., and 120 g. EtBr (XI) in 210 cc. abs. EtOH added, the mixt. refluxed 2-3 hrs. (to a neutral reaction), EtOH removed in vacuo, the residue treated with H2O, and the product isolated by extn. and distn. gave 82% Et .alpha.-p-tolyl-.alpha.-ethyl-.alpha.-cyanoacetate (XII), b1.5 129-31.degree.. XII (148 g.) in 300 cc. abs. EtOH reduced with H and Raney Ni at 60 atm. and 70.degree. gave 73% Et .alpha.-p-tolyl-.alpha.-ethyl-.beta.-aminopropionate (XIII), b0.8 118-22.degree.; picrate m. 165-8.degree. (EtOH). XIII (110.5 g.) in 300 cc. abs. Et2O slowly stirred into 1 l. Grignard soln. (36.5 g. Mg, 165 g. XI) at 0-5.degree., stirred 2 hrs. at 0.degree. and 4 hrs. at ambient temp., held 12 hrs. longer, decompd. with NH4Cl soln., followed by isolation of the product gave 88% 3-p-tolyl-3-ethylazetidin-2-one (XIV), m. 73-6.degree. (petr. ether). XIV (15 g.) and 12 g. LiAlH4 in abs. Et2O, refluxed 5 hrs., cooled to 0.degree., and decompd. with the equiv. amt. of 10% NH4Cl soln. gave 79% 3-p-tolyl-3-ethylazetidine (XV), b0.5 89-91.degree.; picrate m. 208-10.degree. (EtOH); N-carbamoyl deriv. m. 175-8.degree. (EtOH-H2O). XV (5 g.) treated with 15 cc. V gave 80% N-propionyl-3-p-tolyl-3-ethylazetidine, b0.5 140-5.degree.. N-Propionyl-3-phenyl-3-ethylazetidine (15 g.) added dropwise with stirring over a 2-hr. period to 50 cc. fuming HNO3 at -35.degree., the temp. allowed to rise to 15.degree. during 45 min., stirred an addnl. 30 min., poured onto 400 cc. crushed ice, neutralized at less than 10.degree. with solid NaHCO3, and the product isolated and distd. gave 81% N-propionyl-3-(p-nitrophenyl)-3-ethylazetidine (XVI), yellow oil, b0.3 185-95.degree.. XVI (5 g.) in 25 cc. 10% HCl, refluxed 30 min. with 25 cc. concd. HCl, extd. with Et2O, the aq. phase alkalinized with 5% NaOH and further extd. with Et2O, the residue from the second Et2O ext. taken up in abs. EtOH and treated with gaseous HCI gave 2.9 g. crude 3-(p-nitrophenyl)-3-ethylazetidine hydrochloride (XVII), m. 229-31.degree. (abs. EtOH). XVI (5 g.) in 80 cc. abs. EtOH was reduced with H and 3 g. 10% Pd-C at 20.degree. to give N-propionyl-3-(p-aminophenyl)-3-ethylazetidine, b0.3 180-5.degree., which gave with Et2O-HCl N-propionyl-3-(p-aminophenyl)-3-ethylazetidine hydrochloride (hygroscopic), m. 218-20.degree.. XVII (7.8 g.) similarly hydrogenated and hydrolyzed yielded 1.1 g. 3-(p-aminophenyl)-3-ethylazetidine (XVIII), b0.4 135-40.degree.. XVIII gave from Et2O soln. with CO2 the hygroscopic carbonate (XIX), m: 180-2.degree. (decompn.). The structure of XVIII was confirmed by treating 5 g. 3-(p-aminophenyl)-3-ethylazetidin-2-one with 4 g. LiAlH4 in abs. Et2O, refluxing 6 hrs., decompg. with 20% NH4Cl soln., extg. with Et2O, and treating the Et2O soln. with CO2 to obtain a ppt. of XIX, which on acidification and extn. gave XVIII.

Answer 2 CAOLD

L5 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN 1963:415447 HCAPLUS
DN 59:15447
OREF 59:**2745d-e**
TI Production of trimethylethylene oxide
AU Movsumzade, M. M.; Ismailova, F.; Abdullaev, N. G.
SO Azerb. Khim. Zh. (1962), No. 5, 71-6
DT Journal
LA Unavailable
AB As a result of a series of expts. in which the influences of proportion of reagents, time of mixing, catalyst(CoCl2), and inert solvents on the oxidn. of Me2C:CHMe (I) by cold aq. Ca(ClO)2 (II) were evaluated, it was concluded that the max. yield (80-2%) of 2-methyl-2,3-epoxybutane is obtained when I, II, ice, and water (in the ratio of 1:7.5:15:15) are stirred two hrs.

CAOLD Ans. 3

L5 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN 1963:66370 HCAPLUS
DN 58:66370
OREF 58:**11311f-h,11312a-d**
TI Substances acting on the central nervous system. XXVIII. On additional 3-substituted 2-azetidinones
AU Cignarella, Giorgio; Cristiani, Gian F.; Testa, Emilio
CS Lepetit S.p.A., Milan
SO Ann. (1963), 661, 181-7
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. CA 56, 12875f. R'RNCH2CEtPhCO2Et (I) (R = R' = H) (Ia) (CA 53, 6196c) (22 g.), 21 g. PrI, 21 cc. Et3N, and 50 cc. abs. C6H6 refluxed 6 hrs., cooled, treated with 50 cc. H2O, the org. layer sepd., the aq. layer extd. repeatedly with Et2O, the combined org. solns. dried, and fractionated gave 20.5 g. I (R' = Pr, R = H) (II), b0.6 110.degree.. Ia (22 g.), 21 g. iso-PrI, 101 cc. Et3N, and 150 cc. abs. C6H6 heated 8 hrs. at 130.degree. in an N atm. in an autoclave, the contents cooled, filtered, and the filtrate fractionated gave 16 g. crude I (R' = iso-Pr, R = H), b0.15 88.degree.. Ia (22 g.), 16.5 g. BuBr, 20.6 cc. Et3N, and 50 cc. abs. C6H6 refluxed 7 hrs., worked up as above, and redistd. gave 10.8 g. I (R = Bu, R' = H), b0.4 114.degree.. Ia (22 g.) in 20 cc. MeOH added to 11 g. BzH in 15 cc. MeOH, the whole heated 5 min. at 50.degree. kept 12 hrs. at room temp. [concn. in vacuo of a sample gave I (RR' = benzylidene), nondistillable oil], dild. to 150 cc. with MeOH, treated with 40 cc. H2O, hydrogenated over 4 g. 10% Pd-C at room temp. and normal pressure (after 2 hrs. H absorption ceased), filtered, evapd. in vacuo, the residual oil dissolved in Et2O, the soln. dried, and treated with dry HCl gave 15 g. I (R = PhCH2, R' = H) (III) HCl salt, m. 200-3.degree.; pure III.HCl m. 203-6.degree. (reconversion to base and then to III.HCl, then recrystn. from EtOH); from 15 g. III. HCl was isolated 12 g. crude III. EtMgBr soln. (from 5.75 g. Mg in 40 cc. abs. Et2O and 27.5 g. EtBr in 220 cc. abs. C6H6) treated dropwise during 30 min. with 19.5 g. II at 5.degree., the whole stirred 2 hrs. at 0.degree. and 4 hrs. at room temp., treated with 40 cc. cold 2N H2SO4 at 0.degree. the org. layer sepd., the aq. layer repeatedly extd. with C6H6, the combined org. solns. washed neutral, dried, and fractionated gave 23% IV (R = Pr), b0.4 115.degree.. The following IV were similarly prepd. (R, % yield, and b.p./mm. given): iso-Pr, 27, 104.degree./0.4; Bu, 60, 105-10.degree./0.5; PhCH2, 74, 170.degree./0.6. Typical prepns. Method A. 3-Methyl-3-phenyl-2-

azetidinone (T., et al., loc. cit.) (8 g.) and 5.9 g. PhNCO in 80 cc. abs. PhMe refluxed 20 hrs., the soln. concd., the residue heated in vacuo (to 140.degree./1.5 mm.), and the residual product recrystd. from MeOH gave 40% V(R = R'' = Ph, R' = Me), m. 84-5.degree.. Method B. 3-Ethyl-3-phenyl-2-azetidinone (VI) (T., et al., loc. cit.) (10.5 g.) and 7.5 g. PhNCO heated 3 hrs. at 170.degree., the melt cooled, and crystd. from 40 cc. MeOH gave 62% V (R = R'' = Ph, R' = Et), m. 89-91.degree.. The following V were similarly prepd. (R'' = Ph in all cases) (R, R', method, % yield, m.p. given): Ph, H, A, 60, 86-8.degree.; Ph, Et, A, 35, 95-7.degree.; Ph, Pr, A, 23, -- (b1 155-60.degree.); Ph, iso-Pr, A, 37, 127-9.degree.; Ph, Bu, A, 18, 96-7.degree.; Et, Et, A, 79, -- (b1.5 165-70.degree.); Ph, Ph, B, 87, 160-1.degree.. VI (10.5 g.) and 5.94 g. BuNCO in 150 cc. abs. PhMe refluxed 40 hrs. and fractionated gave a forerun, b0.4 110-30.degree., chiefly VI, and 1.25 g. V (R = Ph, R' = Et, R'' = Bu), b0.4 165-70.degree. .nu. 1740, 1700, and 1530 cm.-1 VI (3.5 g.) and 2 cc. 38% aq. HCHO in 35 cc. EtOH heated to boiling, treated dropwise with 1.65 g. pyrrolidine in 5 cc. EtOH, boiled 30 min., evapd. in vacuo, the residual oil dissolved in Et2O, the soln. extd. with 10% HCl, the ext. made alk. with 10% aq. NaOH, and the product isolated with Et2O gave 85% VII (R = Ph, R' = Et, R'' = pyrrolidino), b0.2 140.degree.. The following VII were similarly prepd. (R, R', R,'', % yield, b.p./mm. given): Ph, H, pyrrolidino, 72, 145-50.degree./4; p-MeOC6H4, H, pyrrolidino, 88, 170-5.degree./0.2 (m. 50.5-1.0.degree.); Et, Et, pyrrolidino, 86, 95-100.degree./0.4; Et, Et, Me2N, 85, 125.degree./0.4; Ph, Et, morpholino, 86, 94-5.degree. (Et2O); Ph, Et, 3,3-dimethylazetidino, 72, 135-40.degree./0.4; Ph, iso-Pr, pyrrolidino, 77, 140.degree./0.4; Ph, Bu, pyrrolidino, 45, 140.degree./0.5; Ph, PhCH2, pyrrolidino, 77, -- [m. 130-3.degree. (EtOH)].

L5 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2002 ACS

CAOLD Ans. 3

AN 1963:66369 HCAPLUS
DN 58:66369
OREF 58:**11311a-f**
TI Indoles for comparison with amanita poisons. IV. .beta.-Thioethers of indoles and their preparative desulfurization to phenols
AU Wieland, Theodor; Ruehl, Karl
CS Univ. Frankfurt, Germany
SO Ber. (1963), 96, 260-5
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB Several acetonyl- and acetaldehydethioether phenylhydrazones were converted by rearrangement with alc. HCl to 3-indolyl thioethers. The thioethers from HSCH2CHO desulfurized with Raney Ni gave indoles which were unsubstituted in the pyrrole nucleus. PhSNa treated with ClCH2Ac gave PhSCH2Ac, m. 34-5.degree.. HSCH2CO2Et (I) (36 g.) in 250 cc. dry Et2O treated with 7.2 g. Na and then with cooling and shaking with 28 g. AcCH2Cl, kept 0.5 hr. at room temp., filtered, and distd. yielded 41 g. EtO2CCH2SAc, b3 104.degree.. PhSCH2CH(OEt)2 (II), b2 105-7.degree., was prepd. from BrCH2CH(OEt)2 (III) and PhSNa. II (8 g.) and 30 cc. 1% HCl refluxed 0.5 hr. and extd. with Et2O, and the ext. shaken with powd. NaOAc, filtered, and evapd. gave crude oily PhSCH2CHO. I (12 g.), 20 g. III, and 2.3 g. Na in 100 cc. abs. EtOH refluxed 3 hrs., poured into 250 cc. H2O, and worked up yielded 15 g. EtO2CCH2SCH2CH(OEt)2 (IV), b2 109-11.degree.. IV (12 g.) sapond. with HCl gave EtO2CCH2SCH2CHO. The appropriate S-contg. carbonyl compd. and a suitable phenylhydrazine (equimolar amts.) dild. with AcOH to about 5% concn., kept overnight,

dild. with an equal vol. H2O, and refrigerated yielded 80-90% corresponding RC6H4NHN:CR'CH2SR'' (V) (R, R', R'', and m.p. given): H, Me, Ph, 83.degree.; .omicron.-Me, Me, Ph, 109.degree.; m-Me, Me, Ph, 111.degree.; p-Me, Me, Ph, 96.degree.; m-MeO, Me, Ph, 54.degree.; m-Cl, Me, Ph, 65.degree.; H, Me, EtO2CCH2, 54.degree.; m-Me, Me, EtO2CCH2, 68.degree.; p-Me, Me, EtO2CCH2, 52.degree.; H, H, Ph, 66.degree.; m-Me, H, Ph, 74.degree.; p-Me, H, Ph, 68.degree.; m-MeO, H, Ph, 74.degree.; m-Cl, H, Ph, 72.degree.; p-Me, H, EtO2CCH2, 74.degree.. The appropriate 5% alc. V treated with cooling with dry HCl, filtered after 1 hr., and evapd. or dild. with H2O yielded 80-90% VI (R, R', R'', m.p., and color given): H, Me, Ph, 130.degree., red-brown; 7-Me, Me, Ph, 161.degree., ocher; 6-Me, Me, Ph, 162.degree., light red; 5-Me, Me, Ph, 161-2.degree., ocher; 6-MeO, Me, Ph (VII), 137.degree. (ligroine), pink; 6-Cl, Me, Ph, 142.degree. (AcOH), ocher; H, Me, Et2OCCH2 (VIII), 71.degree., light red; 6-Me, Me, EtO2CCH2, 108.degree., ocher; 5-Me, H, EtO2CCH2, 111.degree. ochre; 6-MeO, Me, EtO2CCH2, 83.degree. (ligroine) light red; H, H, Ph, 154.degree., ocher; 6-Me, H, Ph, 160.degree. (ligroine, red-brown; 5-Me, H, Ph, 156.degree., ocher; 6-MeO, H, Ph (IX), 76.degree., red-brown; 6-Cl, H, Ph (X), 154.degree. (AcOH), light red; 5-Me, H, EtO2CCH2, 71.degree., ocher. All VI were recrystd. from EtOH except where stated otherwise. .omicron.-MeC6H4HNH2, m. 56.degree., p-MeC6H4NHNH2, m. 65.degree., and m-MeC6H4NHNH2, b760 240.degree., were prepd. by the method of Kermack, et al. (CA 16, 98). VIII (1.2 g.) in 15 cc. 10% alc. KOH kept 24 hrs. at room temp. and treated with 2N HCl gave 0.9 g. 2-methyl-3-carboxymethylthioindoline, m. 157.degree. (EtOH). The appropriate VI (1 g.) in 50-100 cc. EtOH refluxed 3 hrs. with 5-10 g. Raney Ni and filtered, the residue boiled twice with EtOH, and the combined alc. solns. evapd. yielded 50-60% 6-methoxy-2-methylindole, m. 102.degree., from VII, 6-methoxyindole, m. 92.degree. (from IX), and 6-chlorindole, m. 78.degree., from X.

L5 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2002 ACS

CAOLD Ans. 4

AN 1962:45914 HCAPLUS
DN 56:45914
OREF 56:**8660i,8661a-i,8662a**
TI Substances acting on the central nervous system. XIV. 3,3-Disubstituted azetidines
AU Testa, I. Emilio; Fontanella, Luigi; Mariani, Luigi; Cristiani, Gian Franco
CS Lepetit S.p.A., Milan
SO Ann. (1960), 633, 56-66
DT Journal
LA Unavailable
AB cf. CA 53, 17958f; 54, 3361h; 54, 3362d; 55, 27270f. I were prepd. and reduced with LiAlH4 to II. Some N-methylazetidines were prepd. from azetidines and MeI or HCO2HCH2O. The NaCNO-3,3-dialkylazetidine reaction gave I (R2 = NH2) (III). A mixt. of 3.22 g. 3-ethyl-3-phenylazetidine and 0.8 g. AcCl was kept at ice-NaCl temp. for 30 min., then at room temp. 1 hr.; decompn. with 10 ml. ice water, extn. with Et2O, and distn. of the washed and dried (Na2SO4) ext. gave 1 g. I (R = Et, R1 = Ph, R2 = Me), b0.4 155-65.degree.. The following I were similarly prepd. (R, R1, R2, and b.p. given): Et, Ph, Et, b0.6 130-50.degree.; Et, Ph, Pr, b0.2 140.degree.; Et, Ph, Bu, b0.5 150.degree.; Et, Ph, iso-Bu, b0.2 145-50.degree.; Et, Ph, Me3C, b0.4 140.degree. [m. 72-4.degree. (ligroine); Et, Ph, CH2Ph, b0.5 190-5.degree.; Et, (CH2)2Ph, b0.3 180-90.degree.; Et, Ph, Ph, -- [m. 63-4.degree. (ligroine)]; Et, Ph, OEt, b1 125-30.degree.; Me, Me, OEt, b24 100-2.degree.. A mixt. of 4.6 g.

3,3-dipropylazetidine and 14 ml. Ac2O was kept at 110-115.degree. for 1 hr., poured into 35 ml. 60.degree. water, brought to pH 6 with Na2CO3 soln., and extd. with Et2O. The ext. was washed (Na2CO3 soln., water), dried (Na2SO4), and distd. to give 4.17 g. I (R = R1 = Pr, R2 = Me), b0.4 96-100.degree.. Similarly the following were prepd. (R, R1, R2, and b.p. given): Me, Ph, Et, b0.4 150-60.degree.; Me, Ph, Me, b0.4 135-40.degree.; Ph, Pr, Et, b0.2 135-45.degree.; Bu, Ph, Me, b0.2 155-65.degree.; Ph, CH2Ph, Me, -- [m. 115-17.degree. (EtOH)]; Ph, CH2Ph, Et, -- [m. 79-80.degree. (aq. EtOH)]; Me, Me, Me, b15 80-90.degree.; Et, Et, Me, b0.4 85-90.degree.; Et, Et, Et, b0.2 85-9.degree.; Bu, Bu, Me, b0.4 108-10.degree.. The following III were prepd. by the acyl halide-Et3N method (R, R1, b.p., and m.p. given): Et, Ph, --, 149-50.degree.; Me, Me, b0.4 180-6.degree., 57-61.degree.; Et, Et, b0.2 200-10.degree., 40-5.degree.. A suspension of 1.5 g. LiAlH4 in 30 ml. abs. Et2O was added dropwise to a soln. of 3 g. I in 20 ml. Et2O, the mixt. was refluxed 3 hrs., treated with 10% NH4Cl at 0.degree., filtered, and the filtrate extd. with Et2O. The dry (Na2SO4) ext. was distd. to give 2.05 g. II (R = Et, R1 = Ph, R2 = Me) (V), b0.6-0.8 75-80.degree.. Similarly the following II were prepd. (R, R1, R2, and b.p. given): Et, Ph, H, b0.4 85-90.degree.; Et, Ph, Pr, b0.2 90.degree.; Et, Ph, Bu, b0.4 98-100.degree.; Et, Ph, iso-Bu, b0.2 95.degree.; Et, Ph, Me3C, b0.3 88-90.degree.; Et, Ph, CH2Ph, b0.2 130.degree.; Et, Ph, (CH2)2Ph, b0.4 150.degree.; Pr, Pr, Me, b21 105-10.degree.; Bu, Bu, Me, b10 103-5.degree.. By the same method the following IV were prepd. (R, R1, and b.p. given): Et, Ph (VI), --[m. 62-4.degree. (EtOH)]; Me, Me (VII), b0.6 100-5.degree.; Et, Et (VIII), b0.2-0.4 135-45.degree.. A suspension of 3 g. LiAlH4 in 30 ml. abs. Et2O was added dropwise to a mixt. of 10 g. 3-ethyl-3-phenylazetidine, 6.3 g. AcOEt, and 50 ml. abs. Et2O, refluxed 150 min., cooled to 0.degree., and decompd. with 5 ml. 10% NH4Cl. The suspension was filtered, the filtrate and the residue were extd. with Et2O and the dried (Na2SO4) ext. was distd. to give 9 g. II (R = Et, R1 = Ph, R2 = Me), b0.7 75-80.degree.. Similarly the following II were prepd. (R, R1, R2, and b.p. given): Et, Ph, Et, b0.4 90-5.degree.; Et, Ph, Ph, b0.4 138-40.degree.; Me, Ph, Me, b0.6 62-5.degree.; Ph, Pr, Me, b0.2 80-2.degree.; Ph, iso-Pr, Me, b0.5-0.6 80-2.degree.; Bu, Ph, Me, b0.6 83-5.degree.; Ph, CH2Ph, Me, b0.5-0.6 130-4.degree.; Ph, cyclohexyl, Me, b0.2-0.3 120-3.degree.; Me, Ph, CH:CHPh, b0.4 130-3.degree.. 3,3-Dimethylazetidine-2H2O (2 g.) treated with 2 ml. MeI in 50 ml. abs. Et2O gave 3.26 g. 1,3,3-trimethylazetidine-HI, m. 138-40.degree.. Similarly, 1,3-dimethyl-3-phenylazetidine-HI, m. 132-5.degree. (decompn.), was obtained from 3-methyl-3-phenylazetidine, 1-methyl-3-ethyl-3-phenylazetidine-HI, m. 131-5.degree. (decompn.), from 3-ethyl-3-phenylazetidine. V treated with MeI gave V.MeI, m. 130.degree. (decompn.). Similarly, VI gave a dimethiodide, m. 100.degree. (decompn.), VII gave a dimethiodide, m. 126-8.degree., and VIII gave a dimethiodide, m. 180-1.degree. (decompn.). II (R = Et, R1 = Ph, R2 = H) was also prepd. from 5 g. 3-ethyl-3-phenylazetidine, 46.5ml. HCO2H, and 3.25 ml. 27.8% CH2O. The mixt. was heated to 105-10.degree. for 150 min., partially evapd. in vacuo, dild. with water, neutralized with Na2CO3, and extd. with Et2O. The ext. was distd. and 2.39 g. product [picrate m. 118-20.degree. (EtOH)] was obtained. A soln. of 5 g. 3-ethyl-3-phenylazetidine in 30 ml. HCO2H heated to 120-30.degree. for 1 hr gave upon distn. 4.4 g. 3-ethyl-3-phenyl-1-formylazetidine, b0.6 125-8.degree., m. 62-4.degree.. 3-Ethyl-3-phenylazetidine (3.2 g.) in 20 ml. N HCl treated with 1.3 g. NaOCN for 15 min. at 50-60.degree. gave 3.6 g. III (R = Et, R1 = Ph), m. 154-6.degree. (5% EtOH). Similarly the following III were prepd. from the corresponding 3,3-dialkylazetidines [R, R1 and m.p. (aq. EtOH unless

specified) given]: Me, Ph, 176.degree.; Ph, Pr, 165-6.degree.; Ph, iso-Pr, 158-60.degree.; Bu, Ph, 129-31.degree.; Ph, CH2Ph, 159-61.degree.; Ph, cyclohexyl, 172-4.degree.; Me, Me, 182-4.degree. (water); Et, Et, 179-80.degree.; Bu, Bu, 114-15.degree..

CAOLD Ans. 4

L5 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN 1962:45913 HCAPLUS
DN 56:45913
OREF 56:**8660h-i**
TI Preparation and reactions of .alpha.-phenyl-.beta.,.beta.-dimethylglycidonitrile and the corresponding amide
AU Young, Raymond Hinchcliffe, Jr.
CS Univ. of Maine, Orono
SO (1961) 75 pp. Avail.: Univ. Microfilms (Ann Arbor, Mich.), Order No. 61-5211
From: Dissertation Abstr. 22, 1834
DT Dissertation
LA Unavailable
AB Unavailable

CAOLD Ans. 5

L5 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN 1962:2337 HCAPLUS
DN 56:2337
OREF 56:**453c-e**
TI 1-Carbamoyl-3-substituted azetidines
IN Testa, Emilio; Fontanella, Luigi; Maffii, Giulio
PA S.p.A., Lepetit
SO Division of Brit. 872,446
DT Patent
LA Unavailable

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 872447		19610712	GB	
	DE 1147585			DE	
	FR 1332510			FR	
	US 3094518		1963	US	

AB (preceding abstr.). The title compds. were prepd. by reaction of a 3-substituted azetidine (Brit. 872,446) with an equimolar amt. of an alkali metal cyanate in H2O at 50-100.degree.. Thus, 32 g. 3-phenyl-3-ethylazetidine in 100 ml. H2O was treated with 100 ml. 2N HCl then 13 g. NaOCN, the mixt. heated 15 min. at 50-60.degree., and cooled to yield 88% 1-carbamoyl-3-phenyl-3-ethylazetidine, m. 154-6.degree. (5% EtOH). The following 1-carbamoylazetidines were prepd. (3,3-substituents, % yield, and m.p. given): Ph, Me (I), 90, 176.degree.; Ph, H, 80, 231-3.degree.; Et, Et, 77, 179-80.degree.; Ph, Pr, 87, 165-6.degree.; Ph, benzyl, 81, 159-61.degree.; Bu, Bu, 90, 114-15.degree.; Ph, Bu, 75, 129-31.degree. Ph, iso-Pr (II), 86, 158-60.degree. Ph, cyclohexyl, 62, 172-4.degree.; and Ph, Me, 64.5, 176.degree.. These compds. were active as sedatives, hypnotics, and antispasmodic agents; the last effect was particularly high with 1-carbamoyl-3-propylazetidine, I, and II, which in doses <20 mg./kg. prevented convulsive seizures induced by pentamethylenetetrazole. The av. lethal dosage, L.D.50. was very high, in all cases exceeding 300-400 mg./kg. on intraperitoneal administration to rats.

CAOLD Ans. 5

L5 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN 1962:2336 HCAPLUS

DN 56:2336
OREF 56:**452i,453a-c**
TI 3-Substituted azetidines
IN Testa, Emilio; Fontanella, Luigi; Maffii, Guilio
PA Lepetit S.p.A.
DT Patent
LA Unavailable

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 872446		19610712	GB	
	DE 1135469			DE	
	FR 1332508			FR	
	US 3076799		1963	US	

AB The title compds. were prepd. from a 2-azetidinone (Brit. 829,663) and LiAlH4 in a molar ratio of 1:0.8-1.5 in an anhyd. inert org. solvent. Thus, 20 g. 3phenyl-3-ethyl-2-azetidinone in 200 ml. anhyd. ether was added slowly to 11 g. LiAIH4 in 100 ml. anhyd. ether, the mixt. refluxed 2.5 hrs., 100 ml. 10% NH4Cl soln. added after cooling (5.degree.), the mixt. extd. with ether, the solvent removed, and the residue distd. to give 13 g. 3-phenyl-3-ethylazetidine, b1.0 85-7.degree.; hydrochloride m. 219-20.degree. (decompn.). The following 3,3-disubstituted azetidines were prepd. (substituents, % yield, m.p. or b.p., and m.p. of hydrochloride given): Et, Et, 70.6, b120-40 84-6.degree., -; Ph, Me (I), 64.2, b0.9 73.degree., 155.degree.; Ph, Pr, 73.5, b0.4 88-90.degree., -; Ph, iso-Pr, 75.3, m. 36-8.degree. (b0.5 81-3.degree.), 244-6.degree. Ph, Bu (II), 73.5, b0.2-0.4 85-90.degree. 128-30.degree.; Ph, benzyl, 85.5, m. 62-4.degree. (b0.2-0.4 136-8.degree.), 171-2.degree.; Ph, cyclohexyl, 74.5, m. 85-7.degree. 210-1.degree.; Ph, Ph, 43, m. 95-6.degree. (b1 160-70.degree.), 245-7.degree.; Et, benzyl, 29, b0.4 120-30.degree. 120-4.degree.; Me, Me, 44.5, b. 90-2.degree., 96-8.degree.; Pr, Pr, 72.4, b20 87.degree., oil; Bu, Bu, 87, b15 110.degree., 96-9.degree.; and Ph (III), 58, b3-3.5 87-9.degree., 78-80.degree.. These compds. possessed useful pharmacol. properties, e.g., III in lab. animals in doses of 1.5-3 mg./kg. caused a very prolonged hypotensive effect, with substantial decrease of the response to adenaline and nordrenaline. Some were active as analgesics, e.g. II, active at doses as low as 10 mg./kg., and some were sympathomimetics, e.g., I. The toxicity of all compds. was reasonably low.

L5 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN 1962:2285 HCAPLUS
CAOLD Ans. 6
DN 56:2285
OREF 56:**434g-i,435a-i,436a-b**
TI Preparation and properties of N-alkylated cyanoethylenimines
AU Wagner-Jauregg, Th.
CS Siegfried Akt.-Ges., Zofingen, Switz.
SO Helv. Chim. Acta (1961), 44, 1237-49
DT Journal
LA German
AB The reaction of BrCH2CHBrCN (I) with aliphatic, cycloaliphatic, and araliphatic amines yielded the corresponding N-alkylated cyanoethylenimines (II). The addn. of HCl or HBr to the II produced 2 series of position-isomeric addn. products. The resulting .alpha.-alkylamino-.beta.-chloropropionitriles (III) reduced ammoniacal AgNO3, while the isomeric .beta.-alkylamino-.alpha.-chloropropionitriles (IV) did not. Some of the III and IV were hydrolyzed to the corresponding amides and carboxylic acids. The addn. of hydrogen halides to the III and

IV yielded new halogenated derivs. of the N-alkyl-.alpha.- and .beta.-alanines. I (42.6 g.) in 60 cc. dry C6H6 treated at 5-10.degree. with 17.5 g. cyclohexylamine (V) and 40.4 g. Et3N in 60 cc. dry C6H6, the mixt. heated 3 hrs. at 80.degree. in a steel bomb, cooled, filtered from 57.3 g. Et3N.HBr, treated with a few mg. 2-C10H7NHPh, concd. in vacuo, and distd. yielded 18 g. N-cyclohexylcyanoethylenimine (VI), m. 39-41.degree. (H2O), b0.005 65-6.degree., n20D 1.4780. VI (10.8 g.), 2.9 g. NaOH, 5 cc. H2O, and 20 cc. EtOH refluxed 1.5 hrs. gave about 7.5 g. (crude) N-cyclohexylethyleniminecarboxylic acid Na salt (VII), m. 266-7.degree. (boiling CH2Cl2). VII (4 g.), 100 cc. 6N HCl, and 100 cc. AcOH refluxed 2 hrs., evapd., boiled with EtOH, filtered, and dild. with Et2O gave 1 g. N-cyclohexyl-.beta.-chloroalanine-HCl, m. 160-2.degree. (iso-PrOH). VI (30 g.) in 160 cc. Et2O reduced with 8.4 g. LiAlH4 in 400 cc. dry Et2O at 0.degree. during 2 hrs. gave 18 g. 1-cyclohexyl-2-aminomethylethylenimine, b18 108-9.degree., n20D 1.4818, which with aq. picric acid gave 2 picrates, m. 86-8.degree. (decompd. at 112.degree.), and 170-2.degree. (aq. EtOH), in approx. 2:1 ratio. VI dissolved at room temp. in 2N HCl and the soln. cooled gave .beta.-chloro-.alpha.-cyclohexylaminopropionitrile-HCl (VIII.HCl), m. 165-7.degree. (decompn.) (MeOH). VII (7.2 g.) in dry Et2O with dry HCl yielded 10.1 g. adduct, m. 141-4.degree., which recrystd. from MeOH gave 3.3 g. VIII.HCl, m. 163-4.degree. (MeOH); the mother liquor concd. to half-vol., dild. with Et2O, and refrigerated gave 2.2 g. .alpha.-chloro-.beta.-cyclohexylaminopropionitrile-HCl (IX.HCl), m. 162-5.degree. (decompn.), sublimed at 120-40.degree./16 mm. V (5.65 g.) in 10 cc. petr. ether treated at 5-10.degree. with 5 g. CH2:CClCN in 10 cc. petr. ether, the mixt. kept 2 hrs. at 0.degree. and 65 hrs. at room temp., and filtered gave 0.45 g. IX.HCl, m. 198-200.degree. (EtOAc-EtOH); 1.1 g. 2nd crop. VIII.HCl (5 g.) and 22.35 cc. 2N KOH dild. with EtOH to soln., kept 3 hrs. at room temp., and worked up gave 1.5 g. basic oil, b0.001 30-8.degree., n20D 1.469, which dissolved in 2N HCl, washed with Et2O, and concd. gave V.HCl, m. 196-8.degree. (EtOH-Et2O). VIII.HCl (2 g.) in 50 cc. 19% HCl heated 3 hrs. at 100.degree., evapd., the residue dissolved in EtOH, and the soln. treated with Et2O gave 0.4 g. NH4Cl and 0.9 g. V.HCl, m. 193-8.degree.. VIII.HCl in aq. Hg(OAc)2 heated, filtered, treated with H2S, filtered again, treated with HCl, and evapd. gave V.HCl. VIII.HCl in H2O treated with NaHCO3, the mixt. extd. with Et2O, the residual VIII (0.75 g.) from the ext. in 10 cc. Et2O added at 0.degree. to 0.76 g. LiAlH4 and 0.16 g. LiH in 40 cc. Et2O-tetrahydrofuran, the mixt. stirred about 3 hrs. at 20.degree., refluxed 3 hrs., kept 1 hr. at room temp., and worked up gave 49 mg. 1-amino-2-cyclohexylaminopropane-HCl (X.HCl), m. 247-52.degree. (abs. EtOH-Et2O). IX (0.62 g.) reduced similarly gave 61 mg. 1-amino-3-cyclohexylaminopropane-HCl, m. 195-9.degree. (EtOH-Et2O). AcH (13.2 g.) added at 0.degree. to 82.5 g. 38% aq. NaHSO3 and the mixt. treated slowly with 29.8 g. V below 30.degree. and then with 19.7 g. KCN in 30 cc. H2O yielded 25.9 g. .alpha.-cyclohexylaminopropionitrile (XI), b20 109-11.degree., n20D 1.4672. XI (10.1 g.) in 50 cc. Et2O reduced during 6 hrs. with 3.8 g. LiAlH4 in 150 cc. dry Et2O gave X, b20 110-12.degree., n20D 1.4759; X HCl, m. 249-52.degree.. V (74.4 g.) treated slowly at 50.degree. with 42.4 g. CH2:CHCN at 65-70.degree., the mixt. kept 3 hrs. at 90.degree., and fractionated gave 105 g. .beta.-cyclohexylaminopropionitrile (XII), b15 132-3.degree., n20D 1.4751. XII (15.2 g.) reduced in the usual manner with LiAlH4 and LiH gave 11.8 g. N-cyclohexylamino-1,3-diaminopropane, b20 127-8.degree.; HCl salt, needles, m. 199-202.degree.. IX.HCl (0.7 g.), 3.15 cc. 2N KOH, and about a 4-fold amt. of EtOH kept 3 hrs., filtered, evapd., the residue dissolved in Et2O, and the soln. distd. gave 0.1 g. crude N-cyclohexylethylenimino

carboxamide (XIII), b0.01 75.degree. (bath), n20D 1.4741; 0.07 g. 2nd crop, b0.01 75-85.degree., n20D 1.4757; both fractions deposited solid XIII, m. 129.5-30.5.degree.. .alpha.-Bromo-.beta.-cyclohexylaminopropionamide-HBr (XIV.HBr) (3 g.) and 75 cc. 16.5% HBr heated 3 hrs. at 100.degree., concd., dissolved in EtOH, the soln. dild. with Et2O, filtered from NH4Br, refrigerated, the pptd. oil dissolved in H2O, and the soln. treated with concd. aq. NaOH gave 0.4 g. XIII, m. 133-5.degree. (C6H6-petr. ether). XIII (250 mg.) in 6.25 cc. 6N HCl and 0.25 cc. AcOH kept at room temp. overnight and evapd. gave 150 mg. .beta.-chloro-.alpha.-cyclohexylaminopropionamide-HCl, m. 196-8.degree. (abs. EtOH). I (106.5 g.), 49.6 g. I, and 101 g. Et3N in 700 cc. C6H6 kept 5.5 hrs. at room temp., filtered from 126.5 g. Et3N.HBr, and worked up yielded 11.8 g. XIV.HBr, m. 181-3.degree. (decompn.) (boiling abs. EtOH). I (74.5 g.) in 180 cc. C6H6 treated at 5.degree. dropwise with stirring with 20.6 g. PrNH2 and 70.6 g. Et3N in 320 cc. C6H6, the mixt. stirred 4 hrs. at room temp., filtered from 60 g. Et3N.HBr, worked up, the oily residue dissolved in 300 cc. 2N HCl, the soln. refrigerated overnight, concd. in vacuo, and dild. with Me2CO gave 1.5 g. NH4Br; the filtrate evapd., the residue dissolved in EtOH, and the soln. dild. with Et2O gave 4 g. ClCH2CH(CONH2)NHPr.HCl, m. 160-3.degree. (abs. EtOH). The mixt. (XV) (3 g.) of the isomeric PhCH2NH derivs. of EtCN in 40 cc. 2N HCl allowed to stand some time, washed with Et2O, and refrigerated overnight yielded 1.3 g. ClCH2CH(CN)NHCH2Ph.HCl (XVI), m. 158.degree. (decompn.) (EtOH). XV (6 g.) in Et2O treated with dry HCl gave 8 g. crude XVI; the mother liquor dild. with Et2O gave PhCH2NHCH2CHClCN.HCl (XVII), decompd. at 162-3.degree. with sintering from 148.degree. (EtOH-Et2O). Hydrolysis of 1.7 g. XVI yielded NH4Cl and 0.35 g. PhCH2NH2.HCl, m. 256-8.degree.. I (74.5 g.) in 180 cc. C6H6 treated dropwise at 5.degree. with stirring with 36.8 g. PhCH2NH2 and 70.6 g. Et3N in 320 cc. C6H6, the mixt. stirred 5 hrs. at room temp., filtered from 57.8 g. Et3N.HBr, treated with a few mg. hydroquinone, kept overnight, filtered again from 5 g. Et3N.HBr. washed, dried, and evapd. gave 14.6 g. PhCH2NHCH2CHBrCN.HBr (XVIII), m. 172-5.degree. (abs. EtOH). XVIII (2 g.) treated in the usual manner with 2N KOH yielded 0.1 g. N-benzylethyleniminecarboxamide, m. 112-14.degree. (C6H6-petr. ether). The infrared absorption spectra of VI, VIII.HCl, IX.HCl, XVI, and XVII were recorded.

L5 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2002 ACS

CAOLD Ans. 6

AN 1962:2284 HCAPLUS
DN 56:2284
OREF 56:**433h-i,434d-g**
TI Reaction of substituted .alpha.-bromoacylophenones with potassium cyanide
AU Suzuki, Takeshi; Yano, Akira; Okada, Masahiko; Ishii, Yoshio
CS Univ. Nagoya
SO Nippon Kagaku Zasshi (1960), 81, 301-5
DT Journal
LA Unavailable
AB Various .alpha.-bromobutyrophenone and .alpha.-bromoacetophenone derivs. were prepd. and the reactions with KCN discussed. New derivs. of butyrophenone used were (substituent and b.p. given): m-Cl, b20 152.degree.; m-Me, b10 114-18.degree.; m-MeO, b10 121.degree.. The following new compds. were used for the reaction with KCN [substituent of BzCHBrEt (I) and m.p. or b.p. given]: p-NO2, m. 73.degree.: m-Cl, b18 180.degree.; m-Me, b10 140-3.degree.; m-MeO, m. 35.degree.; p-HO, m. 86.5-7.5.degree.; m-HO, m. 59.1.degree.. The following new BzCH2Br (II) derivs. were used (substituent and m.p. given): m-Me, 40-40.5.degree.; p-HO, 105-8.degree.. The ketone and KCN were dissolved in 76 vol.-% EtOH

(80 vol.-% EtOH for II derivs.) to obtain solns. approx. 0.05 mole/l.; 25 cc. ketone soln. and 90 cc. KCN soln. were mixed and unreacted CN- was detd. The reaction velocity was 1st order with respect to both KCN and ketone; Arrhenius activation energy and Arrhenius factor were calcd. from the velocity const. (2nd order). The activation energy was high with p-MeO and p-HO derivs. of both ketones, but the Arrhenius factor was about the same. The velocity const. plotted against Hammett's .sigma. gave a good linear relation; .rho. values were + 1.67 for I and +0.75 for II derivs.; p-MeO and p-HO derivs. deviated from the line. Infrared spectra of the products indicated that a mixt. of cis- and trans-ArC(CN).-CHR.O was formed in the normal case, but p-R'OC6H4COCH(CN)R was formed when R' was H or Me. Thus, the reaction was different in these cases, CN- directly attacking the C which had Br in the latter case. The reaction velocity was approx. twice as fast with I derivs. as with II derivs. (attributed to -I effect of the Et group).

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CAOLD Ans. 7

AN 1961:124751 HCAPLUS
DN 55:124751
OREF 55:**23481e-i,23482a-c**
TI Substances acting on the central nervous system. XVIII. 3-Phenylazetidine
AU Testa, Emilio; Fontanella, Luigi; Mariani, Luigi; Cristiani, Gianfranco
CS Lepetit S.p.A., Milan
SO Ann. (1961), 639, 157-65
DT Journal
LA Unavailable
AB cf. CA 55, 7529i. Hydrogenating NCCHPhCO2Et in abs. EtOH and HCl in the presence of 5% Pd-C 30 min. at room temp./1 atm. gave Et .alpha.-phenyl-.beta.-aminopropionate-HCl (I.HCl), m. 164-5.degree.. I (90 g.) and the Grignard compd. from 38.6 g. Mg and 250 g. MeI in 800 ml. Et2O 4 hrs. at 25.degree. gave 51.5% 3-phenyl-2-azetidinone (II), m. 114-16.degree.. II with LiAlH4 in Et2O gave 3-phenylazetidine (III), b3.5 87-9.degree.; picrate m. 149-50.degree.; hydrochloride m. 78-80.degree.; H sulfate m. 110-12.degree.. Treating III with (A) acid chlorides in the presence of Et3N or (B) acid anhydrides yielded N-acyl derivs. The following PhCH.CH2.NR.CH2 (IV) (R = acyl) were thus prepd. (R, method, % yield, and b.p./mm. or m.p. given): Ac, B, 88, 135-7.degree./1; COEt, B, 54, 125.degree./0.6; COPh, B, 75, 131-3.degree./0.4; CO2Et, A, 50, 105-7.degree./0.3; 3,4,5-(MeO)3C6H2CO, A, 69, 109-11.degree.; CONEt2, A, 78, 130-3.degree./0.6; SO3H, A, 60, 185-7.degree. (decompn.); p-MeC6H4SO2, A, 48, 133-6.degree.. IV (R = alkyl), were obtained by (A) reducing IV (R = acyl) with LiAlH4 in Et2O, (B) boiling III in benzene with R halides in presence of Et3N, or (C) boiling 5 g. III and 7.7 g. Et cinnamate with 2.2 g. LiAlH4 in Et2O 2.5 hrs., pouring into 20% NH4Cl, extg. with Et2O, shaking the Et2O layer with 10% HCl, neutralizing the acid layer then with 10% NaOH, and extg. with Et2O. The Et2O ext. worked up gave 30% IV (R = cinnamyl), b0.6 155-60.degree.. Quaternary methiodides were obtained by treating IV (R = alkyl) in Et2O with MeI. The following IV (R = alkyl) and the corresponding MeI salts were thus prepd. [R, method, % yield, b.p./mm. of IV (R = alkyl), and decompn. point of the corresponding MeI salt given]: Me, A, 87, 62-4.degree./2, 137-9.degree.; Et, A(C), 77(56), 110-15.degree./8, 114-16.degree.; CH2Ph, B(C), 64(33), 122-7.degree./0.4, 140-2.degree.; iso-Pr, B, 35, 72-4.degree./0.8, 148-50.degree.; Bu, A, 93, 83-5.degree./0.5, 121-3.degree.; iso-Bu, B, 29, 74-5.degree./0.4, 110-12.degree.; CH2CH:CH2, B, 51, 65.degree./0.3, 115-18.degree.; CH2CO2Et, B, 29, 123-4.degree./0.5, 111-13.degree.; 2,6-Me2C6H3NHCOCH2, B, 53, m. 113-16.degree., -. III (2 g.) in 40 ml. Et2O treated with 2 ml.

MeI yielded 1-methyl-3-phenylazetidine-HI, m. 107-10.degree.. Boiling 1.75 g. III 15 min. with 0.85 g. NaOCN and 13.5 ml. N HCl gave 1.6 g. IV (R = carbamoyl), m. 231-3.degree. (decompn.). Dropwise addn. of 4.45 g. PhNCO to a benzene soln. of 5 g. III gave IV (R = phenylcarbamoyl), m. 202-4.degree.. Leaving 10 g. III and 3.6 g. ethylene oxide in abs. EtOH 86 hrs. at room temp. yielded IV (R = .beta.-hydroxyethyl), b0.8 110-15.degree., which in CHCl3 treated with SOCl2 60 min. at 40-5.degree., cooled, poured into H2O, and the CHCl3 soln. worked up gave IV (R = .beta.-chloroethyl), b0.3 90-3.degree.; hydrochloride m. 136-8.degree.. Adding 6 g. NaNO2 portionwise to a cooled (-5.degree.) soln. of 2.5 g. III in 30 ml. 80% AcOH, raising the temp. slowly to 90.degree., and keeping at this temp. 1 hr. gave 2.1g. IV(R = NO),m. 33-5.degree.. To 3.45g. LiAlH4 in 120 ml. tetrahydrofuran was added dropwise 10 g. IV (R = NO) m 130 ml. tetrahydrofuran, the mixt. stirred 2.25 hrs. at 40-5.degree., and worked up to give IV (R = NH2), b0.5 75-85.degree.; hemimaleate m. 112-14.degree.. Refluxing IV (R = NH2.HCl) in H2O with p-O2NC6H4CHO in EtOH gave IV (R = p nitrobenzylideneamino), m. 112-14.degree..

L5 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2002 ACS

C&OLD Ans. 7

AN 1961:124750 HCAPLUS
DN 55:124750
OREF 55:**23481b-e**
TI Chemistry of ethylenimine. IX. Ring-opening reactions of 1-(p-bromophenylsulfonyl)-2,2-dimethylaziridine
AU Kashelikar, D. V.; Fanta, Paul E.
CS Illinois Inst. of Technol., Chicago
SO J. Org. Chem. (1961), 26, 1841-2
DT Journal
LA Unavailable
AB cf. CA 55, 5449h. Piperidine (I) and PhNH2 (II) added to 1-(p-bromophenylsulfonyl)-2,2-dimethylaziridine (III) with cleavage of the N-primary C bond of the aziridine ring. Pyrolysis of III in PhMe at 150.degree. gave a mixt. of p-bromobenzenesulfonamide (IV) and N-(.beta.-methallyl)-p-bromobenzenesulfonamide (V). Under the same conditions, V also gave IV. In cold, concd. H2SO4, both III and V gave IV. 2,2-Dimethylethylenimine (7.11 g.) and 10.12 g. NEt3 in 50 ml. C6H6 stirred at 0-5.degree. while 25.55 g. p-bromobenzenesulfonyl chloride in 75 ml. C6H6 was added in 1.5 hrs., and the residue distd. gave 22 g. III, m. 81.5-2.5.degree. (EtOAc-ligroine). III (2.9 g.) and 0.86 g. I in 60 ml. C6H6 refluxed 1.5 hrs. gave 2.6 g. N-(1,1-dimethyl-2-piperidylethyl)-p-bromobenzenesulfonamide, m. 106-7.5.degree. (alc.). III (1.45 g.) and 0.47 g. II in 25 ml. C6H6 refluxed 24 hrs. gave 1.39 g. N-(1,1-dimethyl-2-anilinoethyl)-p-bromobenzenesulfonamide, m. 143.5-4.5.degree. (alc.). III and I.HCl in CHCl3 refluxed 2 hrs. gave N-(2-methyl-2-chloropropyl)-p-bromobenzenesulfonamide, m. 127.5-30.0.degree. (alc.). III (2 g.) in 35 ml. PhMe heated 16 hrs. in a bomb gave 0.85 g. IV, m. 165-8.degree.. The mother liquor reduced to a sirup and crystd. gave 0.3 g. V, m. 74.degree. (ligroine). V (0.5 g.) in 20 ml. PhMe similarly heated 16 hrs. gave 0.30 g. IV. N-Phenyl-p-bromobenzenesulfonamide (1 g.) in 25 ml. PhMe similarly heated was recovered unchanged. Either III or V (0.5 g.) stirred 4 hrs. at 0-5.degree. with 10 ml. concd. H2SO4 gave 88-98% IV.